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PATENT  
Attorney Docket No.: MTP-024

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

INVENTOR: Watkins *et al.*  
PATENT NUMBER: 6,936,424 B1  
ISSUE DATE: August 30, 2005  
SERIAL NO.: 09/709,947  
FILING DATE: November 10, 2000  
TITLE: MATERIALS AND METHODS FOR DETECTION AND TREATMENT OF  
BREAST CANCER

Attention: Ms. Marietta Joyce

Certificate of Correction Branch  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**Certificate**  
**OCT 19 2005**  
**of Correction**

**REQUEST FOR CERTIFICATE OF CORRECTION UNDER**  
**35 U.S.C. § 255 and 37 C.F.R. § 1.323**

Sir:

The undersigned wishes to thank Ms. Marietta Joyce for the assistance provided to the undersigned's colleague, Brian R. Chase, during an August 25, 2005 telephone conversation concerning the correction of a typographical error appearing in the priority claim for this patent. It appears that U.S.S.N. 60/165,673, from which this patent claims benefit of an earlier effective filing date under 35 U.S.C. § 119(e), was inadvertently misspelled as "60/165,173." During the August 25, 2005 conversation, Ms. Joyce confirmed our understanding that the typographical error is correctable by a Certificate of Correction.

Accordingly, Matritech, Inc., the assignee of record by virtue of an assignment document recorded on June 8, 2001 at Reel/Frame 011885/0043, requests that the Office issue a Certificate of Correction for U.S. Patent No. 6,936,424 under 35 U.S.C. § 255 and 37 C.F.R. § 1.323. In particular, Matritech requests that the Office issue a Certificate of Correction to replace the application serial number "60/165,173" appearing in section 60 on the face page of the patent and in column 1, line 8 of the patent with application serial number "60/165,673." Furthermore,

10/17/2005 NNGUYEN1 00000076 6936424

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**OCT 21 2005**

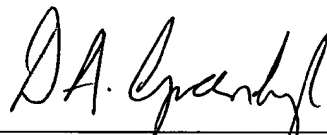
Matritech requests the correction of a printing error appearing in Claim 10 in column 46, line 50 of the patent. In particular, Matritech requests that the text "wherein,the" appearing in issued Claim 10 be corrected to read "wherein the." Issued Claim 10 corresponds to Claim 52, which was introduced during prosecution of the application via an "Amendment and Response" dated December 14, 2004 (copy attached with Claim 52 highlighted).

Matritech submits that the foregoing corrections appear in the enclosed Certificate of Correction (PTO/SB/44 form) and believes that the corrections do not constitute new matter or are of the type that would require re-examination. Matritech respectfully requests that the Office issue a Certificate of Correction reflecting these corrections as they appear on the attached form

A check in the amount of \$100.00 to cover the requisite fee is enclosed. The undersigned believes that no other fee is necessary for entry of this paper. However, if an additional fee is required, the Office is authorized to charge the additional fee to Deposit Account No. 07-1700.

The Office is invited to contact the undersigned with any questions about this submission.

Respectfully submitted,



Duncan A. Greenhalgh  
Reg. No. 38,678  
Attorney for Assignee  
Goodwin Procter, LLP  
Exchange Place  
Boston, Massachusetts 02109

Date: October 12, 2005

Tel. No.: (617) 570-1299  
Fax No.: (617) 523-1231



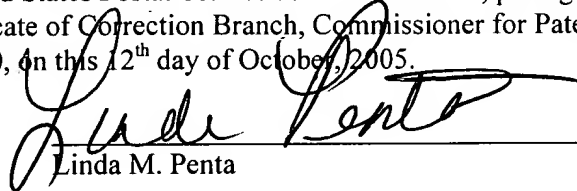
PATENT  
Attorney Docket No. MTP-024

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS: Watkins et al. CONFIRMATION NO.: 3918  
PATENT NO.: 6,936,424 GROUP NO.: 1642  
ISSUE DATE: August 30, 2005 EXAMINER: Alana M. Harris  
TITLE: Materials and Methods for Detection and Treatment of Breast Cancer

**CERTIFICATE OF FIRST CLASS MAILING UNDER 37 C.F.R. 1.8**

I hereby certify that this correspondence, and any document(s) referred to as enclosed herein, is/are being deposited with the United States Postal Service as first class mail, postage prepaid, in an envelope addressed to Certificate of Correction Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 12<sup>th</sup> day of October, 2005.

  
Linda M. Penta

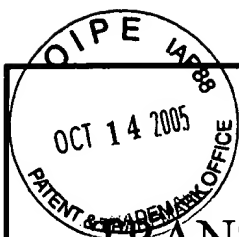
Certificate of Correction Branch  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Submitted herewith is/are:

1. Transmittal Form (1 pg.);
2. Fee Transmittal (1 pg.);
3. Check in the amount of \$100.00;
4. Request for Certificate of Correction (2 pgs.);
5. Certificate of Correction (1 pg.);
6. Copy of Amendment and Response dated December 14, 2004 (12 pgs.);
7. Return receipt postcard

LIBA/2606567v1

OCT 21 2005



# TRANSMITTAL FORM

Application Serial Number	09/709,947
Filing Date	November 10, 2000
First Named Inventor	Watkins
Group Art Unit	1642
Examiner Name	Alana M. Harris
Attorney Docket No.	MTP-024
Patent No.	6,936,424
Issue Date	August 30, 2005

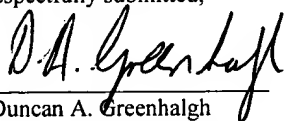
## ENCLOSURES (check all that apply)

<input checked="" type="checkbox"/> Fee Transmittal Form <input checked="" type="checkbox"/> Check Attached <input type="checkbox"/> Copy of Fee Transmittal Form <input type="checkbox"/> Amendment/Response <input type="checkbox"/> Preliminary <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Letter to Official Draftsperson including Drawings [Total Sheets ____] <input type="checkbox"/> Petition for Extension of Time <input type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Form PTO-1449 <input type="checkbox"/> Copies of IDS Citations <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Sequence Listing submission <input type="checkbox"/> Paper Copy/CD <input type="checkbox"/> Computer Readable Copy <input type="checkbox"/> Statement verifying identity of above	<input type="checkbox"/> Copy of Notice to File Missing Parts of Application <input type="checkbox"/> Formal Drawing(s) <input type="checkbox"/> Request For Continued Examination (RCE) Transmittal <input type="checkbox"/> Power of Attorney (Revocation of Prior Powers) <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Executed Declaration and Power of Attorney for Utility or Design Patent Application <input type="checkbox"/> Small Entity Statement <input type="checkbox"/> CD(s) for large table or computer program <input type="checkbox"/> Amendment After Allowance <input checked="" type="checkbox"/> Request for Certificate of Correction <input checked="" type="checkbox"/> Certificate of Correction	<input type="checkbox"/> Notice of Appeal to Board of Patent Appeals and Interferences <input type="checkbox"/> Appeal Brief (in triplicate) <input type="checkbox"/> Status Inquiry <input checked="" type="checkbox"/> Return Receipt Postcard <input checked="" type="checkbox"/> Certificate of First Class Mailing under 37 C.F.R. 1.8 <input type="checkbox"/> Certificate of Facsimile Transmission under 37 C.F.R. 1.8 <input checked="" type="checkbox"/> Additional Enclosure(s) (please identify below) (i) Copy of Amendment and Response filed 12/14/2004
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## CORRESPONDENCE ADDRESS

Direct all correspondence to: Patent Administrator  
Goodwin Procter LLP  
Exchange Place  
Boston, MA 02109  
Tel. No.: (617) 570-1000  
Fax No.: (617) 523-1231  
Customer No. 051414

## SIGNATURE BLOCK

Respectfully submitted,  
  
Duncan A. Greenhalgh  
Attorney for Applicants  
Goodwin Procter LLP  
Exchange Place  
Boston, MA 02109

Date: October 12, 2005  
Reg. No. 38,678  
Tel. No.: (617) 570-1299  
Fax No.: (617) 523-1231

VER 12/00

LIBC/2607817.1

OCT 21 2005

Complete if Known	
Application Serial Number	09/709,947
Filing Date	November 10, 2000
First Named Inventor	Watkins
Group Art Unit	1642
Examiner Name	Alana M. Harris
Attorney Docket No.	MTP-024

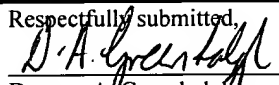
  

**FEES TRANSMITTAL**

FY 2005

OCT 14 2005

PATENT & TRADEMARK OFFICE

METHOD OF PAYMENT	FEE CALCULATION (continued)																																																																																																
<p>1. <input checked="" type="checkbox"/> Payment Enclosed:  <input checked="" type="checkbox"/> Check <input type="checkbox"/> Money Order <input type="checkbox"/> Other</p> <p>2. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to credit or charge any fee indicated below for this submission to Deposit Account No. 07-1700.  <input type="checkbox"/> Required Fees (copy of this sheet enclosed).  <input checked="" type="checkbox"/> Additional fee required under 37 CFR 1.16 and 1.17.  <input checked="" type="checkbox"/> Overpayment Credit.</p> <p>3. <input checked="" type="checkbox"/> Applicant claims small entity status.</p>	<p>3. ADDITIONAL FEES</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th>Large Entity Fee (\$)</th> <th>Small Entity Fee (\$)</th> <th>Fee Description</th> <th>Fee Paid</th> </tr> </thead> <tbody> <tr><td>130</td><td>65</td><td>Surcharge - late filing fee or oath</td><td></td></tr> <tr><td>50</td><td>25</td><td>Surcharge - late provisional filing fee or cover sheet</td><td></td></tr> <tr><td>130</td><td>130</td><td>Non-English specification</td><td></td></tr> <tr><td>2,520</td><td>2,520</td><td>Request for ex parte reexamination</td><td></td></tr> <tr><td>120</td><td>60</td><td>Extension for reply within first month</td><td></td></tr> <tr><td>450</td><td>225</td><td>Extension for reply within second month</td><td></td></tr> <tr><td>1020</td><td>510</td><td>Extension for reply within third month</td><td></td></tr> <tr><td>1590</td><td>795</td><td>Extension for reply within fourth month</td><td></td></tr> <tr><td>2160</td><td>1080</td><td>Extension for reply within fifth month</td><td></td></tr> <tr><td>500</td><td>250</td><td>Notice of Appeal</td><td></td></tr> <tr><td>500</td><td>250</td><td>Filing a brief in support of an appeal</td><td></td></tr> <tr><td>1000</td><td>500</td><td>Request for oral hearing</td><td></td></tr> <tr><td>400</td><td>400</td><td>Petitions to the Commissioner (Gp. I)</td><td></td></tr> <tr><td>200</td><td>200</td><td>Petitions to the Commissioner (Gp. II)</td><td></td></tr> <tr><td>130</td><td>130</td><td>Petitions to the Commissioner (Gp. III)</td><td></td></tr> <tr><td>180</td><td>180</td><td>Submission of Information Disclosure Statement</td><td></td></tr> <tr><td>790</td><td>395</td><td>Filing a submission after final rejection (37 CFR 1.129(a))</td><td></td></tr> <tr><td>790</td><td>395</td><td>For each additional invention to be examined (37 CFR 1.129(b))</td><td></td></tr> <tr><td>100</td><td>100</td><td>Certificate of Correction for applicant's error</td><td>100.00</td></tr> <tr><td>130</td><td>65</td><td>Submission of Terminal Disclaimer</td><td></td></tr> <tr><td colspan="2">Other fee (Specify)</td><td></td><td></td></tr> <tr><td colspan="2">Other fee (Specify)</td><td></td><td></td></tr> </tbody> </table>	Large Entity Fee (\$)	Small Entity Fee (\$)	Fee Description	Fee Paid	130	65	Surcharge - late filing fee or oath		50	25	Surcharge - late provisional filing fee or cover sheet		130	130	Non-English specification		2,520	2,520	Request for ex parte reexamination		120	60	Extension for reply within first month		450	225	Extension for reply within second month		1020	510	Extension for reply within third month		1590	795	Extension for reply within fourth month		2160	1080	Extension for reply within fifth month		500	250	Notice of Appeal		500	250	Filing a brief in support of an appeal		1000	500	Request for oral hearing		400	400	Petitions to the Commissioner (Gp. I)		200	200	Petitions to the Commissioner (Gp. II)		130	130	Petitions to the Commissioner (Gp. III)		180	180	Submission of Information Disclosure Statement		790	395	Filing a submission after final rejection (37 CFR 1.129(a))		790	395	For each additional invention to be examined (37 CFR 1.129(b))		100	100	Certificate of Correction for applicant's error	100.00	130	65	Submission of Terminal Disclaimer		Other fee (Specify)				Other fee (Specify)							
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<p style="text-align: center;"><b>CORRESPONDENCE ADDRESS</b></p> <p>Direct all correspondence to:</p> <p>Patent Administrator  Goodwin Procter LLP  Exchange Place  Boston, MA 02109  Tel. No.: (617) 570-1000  Fax No.: (617) 523-1231  Customer No. 051414</p>	<p style="text-align: center;"><b>SIGNATURE BLOCK</b></p> <p>Respectfully submitted,    Duncan A. Greenhalgh  Attorney for the Applicants  Goodwin Procter LLP  Exchange Place  Boston, MA 02109</p> <p>Date: October 12, 2005  Reg. No.: 38,678  Tel. No.: (617) 570-1299  Fax No.: (617) 523-1231</p>																																																																																																

UNITED STATES PATENT AND TRADEMARK OFFICE  
**CERTIFICATE OF CORRECTION**

PATENT NO. : 6,936,424 B1  
DATED : August 30, 2005  
INVENTOR(S) : Watkins *et al.*

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

On the face of the patent, in section (60), delete "60/165,173, filed on Nov. 12, 1999" and insert --60/165,673, filed on Nov. 16, 1999--.

In column 1, line 8, delete "60/165,173, filed Nov. 12, 1999" and insert --60/165,673, filed Nov. 12, 1999--.

In Claim 10, column 46, line 50, delete "wherein,the" and insert --wherein the--

MAILING ADDRESS OF SENDER: Patent Administrator PATENT NO.: 6,936,424 B1  
Goodwin Procter LLP  
Exchange Place  
Boston, MA 02109  
Tel. No.: (617) 570-1000  
Customer No. 051414

OCT 21 2005



PATENT  
Attorney Docket No. MTP-024

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT(S): Watkins *et al.* CONF. NO.: 3918  
SERIAL NO.: 09/709,947 GROUP NO.: 1642  
FILING DATE: November 10, 2000 EXAMINER: Harris, Alana M  
TITLE: Materials and Methods for Detection and Treatment of Breast  
Cancer

Mail Stop RCE  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**AMENDMENT AND RESPONSE**

Sir:

Responsive to the Office Action for the above-identified patent application, made final, mailed from the Office on June 14, 2004, please extend the deadline for response by three months up to and including December 14, 2004. Applicants enclose a petition and a check to cover the extension fee. If any further fee is required, please debit Deposit Account No. 20-0531.

**Amendments to the Claims** are reflected in the listing of claims, which begins on page 2 of this paper.

**Remarks** begin on page 6 of this paper.

## AMENDMENTS TO THE CLAIMS

Claims 1-40, 44, 49 and 56-62 were cancelled previously. Claims 41-42 and 55 have been cancelled herein without prejudice to their subsequent reintroduction into this application or their introduction into a related application. Claims 43, 45, 46, 48, 50, 51 and 54 have been amended. New claims 63-71 have been added.

1-42. (Cancelled)

43. (Currently amended) A method of diagnosing breast cancer in a mammal, the method comprising the steps of:

(a) obtaining a sample isolated from the mammal; and

(b) detecting in the sample the presence or absence of a protein characterized as comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 1; SEQ ID NO: 2; SEQ ID NO: 3; SEQ ID NO: 4; and SEQ ID NO: 5; ~~SEQ ID NO: 6;~~ ~~SEQ ID NO: 7;~~ ~~SEQ ID NO: 8;~~ ~~SEQ ID NO: 9;~~ ~~SEQ ID NO: 10;~~ ~~SEQ ID NO: 11;~~ ~~SEQ ID NO: 12;~~ ~~SEQ ID NO: 13;~~ ~~SEQ ID NO: 14;~~ ~~SEQ ID NO: 15;~~ ~~SEQ ID NO: 16;~~ ~~SEQ ID NO: 17;~~ ~~SEQ ID NO: 18;~~ ~~SEQ ID NO: 19;~~ ~~SEQ ID NO: 20;~~ ~~SEQ ID NO: 21;~~ ~~SEQ ID NO: 22;~~ and SEQ ID NO: 23, which if present is indicative of breast cancer in the mammal, wherein the presence of the protein is indicative of the presence of breast cancer in the mammal, and wherein the absence of the protein is indicative of the absence of breast cancer in the mammal.

44. (Cancelled)

45. (Currently amended) The method of claim 43 or 70, wherein the sample comprises breast tissue.

46. (Currently amended) The method of claim 43 or 70, wherein the sample comprises a body fluid.



47. (Original) The method of claim 46, wherein the body fluid is selected from the group consisting of blood, serum, plasma, sweat, tears, urine, peritoneal fluid, lymph, vaginal secretions, semen, spinal fluid, ascitic fluid, saliva, sputum, and breast exudate.

48. (Currently amended) A method of diagnosing breast cancer in a mammal, the method comprising the steps of:

(a) contacting a sample derived from the mammal with a binding moiety that binds specifically to a protein comprising an amino acid sequence ~~selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 5, SEQ ID NO: 22, and SEQ ID NO: 23,~~ thereby to produce a complex; and

(b) detecting the presence or absence of a complex, wherein the presence of the complex is indicative of the presence of breast cancer in the mammal, and wherein the absence of the complex is indicative of the absence of breast cancer in the mammal.

49. (Cancelled)

50. (Currently amended) The method of claim 48 or 71, wherein the binding moiety is selected from the group consisting of an antibody, an antibody fragment and a biosynthetic antibody binding site.

51. (Currently amended) The method of claim 48 or 71, wherein the binding moiety is an antibody.

52. (Original) The method of claim 51, wherein the antibody is a monoclonal antibody.

53. (Original) The method of claim 50, wherein the binding moiety is labeled with a detectable moiety.

54. (Currently amended) The method of claim 48, wherein the absence of a detectable amount of the ~~protein~~ complex is indicative of the absence of breast cancer.

55-62. (Cancelled)

63. (New) The method of claim 46, wherein the body fluid is serum.

64. (New) The method of claim 48 or 71, wherein the sample comprises breast tissue.

65. (New) The method of claim 48 or 71, wherein the sample comprises a body fluid.

66. (New) The method of claim 65, wherein the body fluid is selected from the group consisting of blood, serum, plasma, sweat, tears, urine, peritoneal fluid, lymph, vaginal secretions, semen, spinal fluid, ascitic fluid, saliva, sputum, and breast exudate.

67. (New) The method of claim 65, wherein the body fluid is serum.

68. (New) The method of claim 43, wherein the presence of a detectable amount of the protein is indicative of the presence of breast cancer in the mammal.

69. (New) The method of claim 43, wherein the absence of a detectable amount of the protein is indicative of the absence of breast cancer in the mammal.

70. (New) A method of diagnosing breast cancer in a mammal, the method comprising the step of:

determining whether a protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, and SEQ ID NO:5 is present in a sample derived from the mammal in an amount greater than or equal to a threshold value indicative of the presence of breast cancer in the mammal,

wherein an amount of protein greater than or equal to the threshold value is indicative of the presence of breast cancer in the mammal and an amount of protein less than the threshold value is indicative of the absence of breast cancer in the mammal.

71. (New) A method of diagnosing breast cancer in a mammal, the method comprising the steps of:

(a) contacting a sample from the mammal derived from the mammal with a binding moiety that binds specifically to a protein comprising an amino acid sequence of SEQ ID NO:5, thereby to produce a complex; and

(b) determining whether the complex is present in an amount greater than or equal to a threshold value indicative of the presence of breast cancer in the mammal,

wherein an amount greater than or equal to the threshold value is indicative of the presence of breast cancer in the mammal and an amount less than the threshold value is indicative of the absence of breast cancer in the mammal.

## REMARKS

Claims 41, 42 and 55 have been cancelled without prejudice to Applicants' right to prosecute the claimed subject matter in the present application and in related applications. Claims 43, 45, 46, 48, 50, 51 and 54 have been amended. New claims 63-71 have been added. Upon entry of this paper, claims 43, 45-48, 50-54, and 63-71 will be pending and under consideration in this application.

### Interview

At the outset, Applicant's representative, Duncan Greenhalgh, wishes to thank Examiners Harris and Eyler for the courtesy extended and for the Examiners' insightful comments during the in-person interview with Duncan Greenhalgh at the Office on December 7, 2004. The substance of the interview is discussed in the Interview Summary provided by the Office on December 7, 2004. In addition, the substance of the interview is incorporated in this paper. As indicated in the Interview Summary, Applicants requested rejoinder of proteins identified by SEQ ID NOs: 1-5, because SEQ ID NO:5 reflects the sequence of the protein U2 snRNP B" and SEQ ID NOs: 1-4 are fragments of U2 snRNP B". The Office agreed that SEQ ID NOs: 1-5 would be searched and examined.

### Claim amendments

Applicants have amended claim 43 to remove unnecessary wording and to recite a method wherein the presence of a protein is indicative of the presence of breast cancer in a mammal and wherein the absence of the protein is indicative of the absence of breast cancer in the mammal. Applicants have amended claim 48 to remove unnecessary wording and to recite a method wherein the presence of a complex is indicative of the presence of breast cancer in a mammal and wherein the absence of the complex is indicative of the absence of breast cancer in the mammal. Support for the amendments to claims 43 and 48 is found in the application as originally filed, for example, in the paragraph bridging pages 6 and 7; in the first paragraph on page 14; in the last paragraph on page 36; and in original claim 54.

Applicants have amended claims 45, 46, 50 and 51 to alter claim dependency. Applicants have amended claim 54 for consistency with claim 48, from which it depends.

Support for new claims 63 and 67 can be found in the application as originally filed, for example, in original claim 14. Support for new claim 64 can be found in the application as originally filed, for example, in original claim 11. Support for new claim 65 can be found in the application as originally filed, for example, in original claim 12. Support for new claim 66 can be found in the application as originally filed, for example, in original claim 13. Support for new claims 68 and 69 can be found in the application as originally filed, for example, in the paragraph bridging pages 6 and 7; in the paragraph bridging pages 11 and 12; in the first paragraph on page 14; in the last paragraph on page 36; and in original claim 54. Support for new claim 70 can be found in the application as originally filed, for example, in the paragraph bridging pages 6 and 7; and in original claims 43, 44, 54 and 55. Support for new claim 71 can be found in the application as originally filed, for example, in the paragraph bridging pages 6 and 7; and in original claims 48, 49, 54, and 55.

Applicants submit that the amendments introduce no new matter.

The following comments address in order the remaining issues raised in the Office action.

*Information Disclosure Statement*

During the in-person interview on December 7, 2004, Applicant's representative was informed that the Office had received the Information Disclosure Statements resubmitted to the Office on April 6, 2004. Applicants request that the Office consider the art identified in the PTO-1449 forms and confirm this by initialing each entry on the PTO-1449 forms. Applicants request that the Office then provide a copy of each of the initialed PTO-1449 form for completion of Applicants' files.

Claim Rejections Under 35 U.S.C. § 102(e)

According to section 9 of the outstanding Office Action, claims 41-43, 45-48 and 50-55 presently stand rejected under 35 U.S.C. § 102(e), as allegedly anticipated by U.S. Patent Application Publication number 2002/0081659 ("Rosen"), noting that sequence 687 of Rosen comprises SEQ ID NO: 1 of the present application and that the five hundred forty-fifth paragraph of Rosen mentions breast cancer. Claims 41, 42 and 55 have been cancelled thereby obviating this rejection with respect to these claims. Applicants respectfully traverse this rejection to the extent that it is maintained over claims 43, 45-48 and 50-54, as amended, for the following reasons.

Applicants submit that it is well settled that, for a reference to anticipate a claim under 35 U.S.C. 102(e), the "reference must clearly and unequivocally disclose the claimed compound or direct those skilled in the art to the compound without *any* need for picking, choosing, and combining...." *In re Arkley*, 455 F.2d 586, 587 (CCPA 1972) (emphasis in original). A § 102 rejection is "proper only when the claimed subject matter *is* identically disclosed or described in 'the prior art.'" *Id.* at 587 (emphasis in original). Furthermore, Applicants submit that it is well settled law that a "claimed invention cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled." *Amgen v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1354 (Fed. Cir. 2003). *See also In re Donohue*, 766 F.2d 531 (Fed. Cir. 1985) (holding that a non-enabled disclosure does not constitute prior art under 35 U.S.C. § 102).

Applicants respectfully submit that Rosen does not describe that the protein identified by sequence number 687 is a marker for breast cancer because it fails to point to this particular combination without random "picking, choosing, and combining" from a group appearing to contain four hundred fifty-nine sequences, several hundred possible indications, and four possible uses. Furthermore, because Rosen fails to enable one skilled in the art to make or use a protein identified by sequence number 687 as a marker for breast cancer, it cannot anticipate the present application under 35 U.S.C. § 102(e). Each of these issues is addressed in more detail below.

I. Rosen does not describe that sequence number 687 can be used a marker for breast cancer without random "picking, choosing, and combining."

The Arkley court held that a rejection under 35 U.S.C. § 102 is only proper when "the claimed subject matter *is* identically disclosed or described in 'the prior art.'" Id. at 587 (emphasis in original). The Arkley court further held that for a "rejection under 35 U.S.C. § 102(e) to have been proper, the . . . reference must clearly and unequivocally disclose the claimed [invention] or direct those skilled in the art to the [invention] without *any* need for picking, choosing, and combining various disclosures not directly related to each other by the teachings of the cited reference." Id. (emphasis in original). In reversing a claim rejection under 35 U.S.C. § 102(e), the Arkley court referred to In re Ruschig, 379 F.2d 990 (CCPA 1967), which analogized an invention to a particular tree in a forest and held an application did not describe a particular invention where the application lacked "blaze marks which single out particular trees." Ruschig at 995. In Ruschig, the applicants claimed N-(p-chlorobenzenesulfonyl)-N-propylurea, yet they only disclosed a general class of benzenesulfonylureas with two substituents, one of which can be placed in each of the three positions on the benzene ring. Id. at 991, 994. The Examiner calculated that at least 1,010 compounds were disclosed by this description. Id. at 994. The Ruschig court held, therefore, that "while [...] naming is not essential, something more than the disclosure of a class of 1000, or 100, or even 48, compounds is required." Id. The appellants argued that "guides" to N-(p-chlorobenzenesulfonyl)-N-propylurea were provided in the specification, for example, by listing one particular substituent together with 18 others. Id. at 995. The Ruschig court found this argument unpersuasive because it did not lead one to conclude that one substituent was preferred to the other 18. Id. at 995. The Ruschig court held, therefore, that N-(p-chlorobenzenesulfonyl)-N-propylurea was not adequately described in the specification and affirmed the rejection of the claimed subject matter. Id. at 995, 996.

Similarly, Rosen does not "clearly and unequivocally" describe that the protein identified by sequence number six hundred eighty-seven is a marker for breast cancer, nor does it guide one skilled in the art to it. To illustrate the analogy with Ruschig, it may be helpful to consider the Rosen reference as describing a method with three independent substituents: a sequence, an

indication, and a possible use. The "substituent" space in Rosen includes four hundred fifty-nine polypeptide sequences, an estimated several hundred indications (listed in paragraphs 425-548), and up to four possible uses for each indication: diagnosis, prognosis, prevention, and treatment. Similar to Ruschig, nowhere in Rosen is sequence number 687 pointed out as associated with breast cancer and nowhere is it indicated that this sequence can be used for the diagnosis (as opposed to prognosis, prevention, or treatment) of breast cancer. "Breast cancer," for example, is listed in paragraph 545 of Rosen which also appears to contain 70 other indications. This particular paragraph alone appears to provide no fewer than 130,356 possibilities (459 sequences x 71 indications x 4 uses). Applicants estimate the total number of possible indications listed between paragraphs 425-548 of Rosen application to be several hundred. Conservatively, Rosen appears to teach at least several hundred thousand different possibilities.

Applicants submit that Rosen does not reasonably lead a person skilled in the art to any particular sequence associated with either diagnosis, prognosis, prevention, or treatment of any particular indication without random "picking, choosing, and combining." In fact, Rosen fails to provide guidance to a single combination of the elements discussed above. Applicants fail to see any "blaze marks" provided in the Rosen application that would lead anyone to reasonably believe that sequence number 687 was "preferred" as a tool for detection of breast cancer. In contrast to Rosen, the present application "clearly and unequivocally" identifies the use of protein of SEQ ID NO: 5 and fragments thereof (namely the proteins of SEQ ID NO: 1-4) as markers for breast cancer.

Because the Rosen application does not "clearly and equivocally" describe diagnosing breast cancer in a mammal using a protein comprising any of SEQ ID NOS: 1-5 as a marker, Applicants submit that the Rosen application cannot anticipate the claimed invention.



II. Rosen does not enable the use of any of Applicants' SEQ ID NOs:1-5 as a marker for breast cancer.

For a reference to be enabling, it is well settled that a person skilled in the art should be able to practice the invention without "undue experimentation." MPEP 2164.01. See also In re Wands, 858 F.2d 731 (Fed. Cir. 1988). The factors courts consider when determining whether experimentation is "undue" include, but are not limited to: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. MPEP 2164.01(a).

When this test is applied to Rosen, Applicants submit that Rosen clearly does not enable one skilled in the art to practice using an amino acid sequence comprising any of Applicants' SEQ ID NOs: 1-5 as a marker for breast cancer without "undue experimentation." Addressing factors (A) and (B), Applicants submit that in order for Rosen to anticipate the claimed invention, Applicants submit that Rosen needs to identify the use of a protein comprising any of Applicants' SEQ ID NOs: 1-5 as a marker for breast cancer. As discussed in section I, Applicants submit that Rosen fails to do this. Addressing factor (F), Rosen provides no direction concerning the use of sequence number 687, Rosen's amino acid sequence apparently comprising Applicants' SEQ ID NO:1, or any other sequence comprising any of SEQ ID NOS: 1-5 as a marker for breast cancer. As discussed above, there are at least hundreds of thousands of possible combinations of sequences, possible indications, and possible uses based on the teachings of Rosen, and that there is no teaching whatsoever leading the skilled artisan to combine the protein of sequence number 687 and breast cancer diagnosis. Addressing factor (G), there are no working examples of the use of a protein comprising any of Applicants' SEQ ID NOs:1-5 as a breast cancer marker. There is not even a prophetic example that the protein of sequence 687 can be used as a breast cancer marker. Addressing factor (H), in view of the absence of specific guidance in Rosen pointing specifically to the use of a protein comprising any of Applicants' SEQ ID NOs:1-5 as a breast cancer marker, Applicants submit that the quantity of

experimentation needed to practice the present invention based on the content of the Rosen disclosure is very large, as one of skill in the art would need to test each sequence disclosed in Rosen for each recited possible indication and for each recited possible use before learning which combinations were of any use. Addressing factors (C)-(E), Applicants submit that based on the level of ordinary skill in the art, the state and unpredictability of the art, and the lack of direction provided by Rosen, the usefulness of a protein comprising any of Applicants' SEQ ID NOs:1-5 as a breast cancer marker was not predictable absent the specific teachings of the present application. Applicants submit, therefore, that Rosen does not enable one skilled in the art to use a protein comprising any of Applicants' SEQ ID NOs:1-5 as a marker for breast cancer as required by Amgen and, therefore, does not qualify as prior art under 35 U.S.C. § 102(e).

In summary, Applicants respectfully submit that Rosen does not qualify as an anticipatory reference under 35 U.S.C. § 102(e) because it does not describe the invention as required by Arkley, and because it does not enable the invention as required by Amgen. Accordingly, Applicants respectfully request that the rejection of pending claims 43, 45-48, and 50-54 be reconsidered and withdrawn.

### CONCLUSION

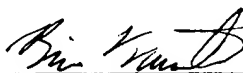
Applicants believe that the claims are in condition for immediate allowance. The Examiner is invited to telephone the undersigned attorney to discuss any remaining issues.

Respectfully submitted,

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